REMARKS

Claims 1 and 5 are pending in the instant application. Claims 1 and 5 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. 112, First Paragraph

Claim 1 has been rejected under 35 U.S.C. 112, first paragraph because the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner suggests that claim 1 recites "non-viral" cells but no reference was given in the specification to support this amendment to the claims. Applicants respectfully traverse this rejection.

Applicants respectfully point out that in the reply filed August 23, 2005, at page 6, Applicants stated "claim 1 has been amended to recite that the cells being contacted are non-viral cells, as taught in the specification as filed at pages 9-18". Therefore, contrary to the Examiner's suggestion, Applicants provided a specific reference to the specification for support of the amendment. If one of skill reviews the disclosure at pages 9-18 it is clear that the instant invention involves contact of cells that are not viral cells but are tumor cells or hyperproliferating non-viral cells. Nowhere in the specification as filed is there any reference to contact of viral cells. Therefore, one of skill would understand that the instant invention involves contact of the cells types taught in the

specification as filed, which are always non-viral cells. Moreover, one of skill in the art would understand the definition of a non-viral cell and be able to apply the instant invention. Accordingly, claim 1 meets the requirements of 35 U.S.C. 112, first paragraph. Withdrawal of this rejection is respectfully requested.

II. Rejection Under 35 U.S.C. 102

The rejection of claims 1 and 5 under 102(b) as being anticipated by Qui et al. ((1996) *J. Biol. Chem.* 271:31915-31921) has been maintained for reasons of record. It is suggested that Qui et al. teach a method of stabilizing or maintaining the redox state of hypoproliferative human colonic carcinoma cells, cell line HCT116, by contact the cells with chemotherapeutic agents, aziridinylbenzoquinones, and a redox clamping agent, N-acetylcysteine. It is suggested that this reference teaches redox cycling in abnormal growth or proliferation and that the effect of N-acetylcysteine on free radical production by the quinines suggests effective transfer of the radical character from an oxygen-centered radical to a less reactive sulfur-center radical (Reaction 2). Further, in response to Applicants arguments, the Examiner suggests that fluctuations of redox state appear to regulate transcription of genes that control proliferation and that an interrelationship exists between the redox state and growth control, with N-acetylcysteine resulting in a more reducing redox state of some proliferating cells. The Examiner further suggests that "The system, as disclosed by Qui, is dynamic with p21 a critical site of redox regulation. The exposure of HCT116 cells to NAC [N-acetylcysteine] caused an

increase in p21 (a cell cycle regulating gene) mRNA and thus contributed to the effects of AZQ as an antitumor agent. Applicants respectfully disagree with the Examiner's conclusions regarding this reference.

As discussed in the previous response dated March 24, 2006, Qui et al. disclose the mechanism of action of aziridinylbenzoquinones. This reference teaches that the metabolism of aziridinylbenzoquinones generates oxygen radicals. In turn, these oxygen radicals induce expression of the cell cycle inhibitor p21 whose overexpression suppresses the growth of tumor cells. See first and third paragraph of the abstract. Qui et al. further teach inhibiting aziridinylbenzoquinone-mediated induction of p21 using the antioxidant N-acetylcysteine, not increasing induction of p21 as suggested by the Examiner. This is most easily seen in Figure 7, page 31919. In this figure, treatment of cells with N-acetylcysteine results in less induction of p21 when cells are also treated with the various drugs. It is only in the control cells, those not treated with AZQ that N-acetylcysteine had any effect on p21 that was an inductive effect. This inhibition of p21 induction is suggested to result from oxidation of the thiol of N-acetylcysteine by the free radicals formed during the metabolism of the aziridinylbenzoquinones. Therefore, this reference fails to teach *sensitizing* non-viral cells to the effects of a chemotherapeutic agent using a redox clamping agent because the antioxidant of Qui et al. blocks the aziridinylbenzoquinones-mediated induction of p21. The reference instead teaches the opposite effect, decreasing the desired effect of the chemotherapeutic agent. Accordingly, this reference fails to

teach each and every element of the instant claims and therefore fails to anticipate the present invention. It is therefore respectfully requested that this rejection be withdrawn.

III. Conclusion

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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Date: **September 25, 2006**

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